

CRRT in patients with HIV/AIDS

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Abstract

Background: AKI is a common complication among human immunodeficiency virus (HIV)-infecting patients and resulting in increased morbidity and mortality. CRRT is a useful method and instrument in critically ill patients with fluid overload and metabolic disarray, especially in those who are unable to tolerate the intermittent hemodialysis. However, the epidemiology, influence factors of CRRT and mortality in patients with HIV/AIDS are still unclear in China. This study aims to study the HIV-infected patients admitted in ICU and explore the influence factors correlated with CRRT and prognosis.

Methods: We performed a retrospective case-control study, in ICU of Beijing Ditan Hospital Capital Medical University, which is a top three hospital majoring in infectious diseases. From June 1,2005 to May 31,2017, 225 cases were enrolled in this research eventually.

Results: 122(54.2%) patients were diagnosed with AKI during their stay in ICU, the number and percentage of AKI stage 1/2/3 were respectively 38(31.1%)/23(18.9%)/61(50%). 26.2% of AKI patients received CRRT during the stay of ICU. 56.25% CRRT patients died in ICU. The 28-day mortality was 62.5%, and the 90-day mortality was 75%. By multivariate logistics analysis, it showed that the use of vasoactive agents (OR=174.31,95% CI 1.743-65.271, p=0.018), diagnosis of PCP(OR=27.136,95% CI 1.855-397.066, p=0.016) and longer duration of CRRT (OR=1.034,95% CI 1.004-1.065, p=0.028) were independent risk factors for predicting patients' death of CRRT in ICU. The Cox Analysis for the cumulative survival of AKI 3 patients between the CRRT and non-CRRT groups shows no significant differences (p =0.309).

Conclusions: The incidence of AKI was 54.2% in HIV-infected patients admitted to the ICU, and about 26.2% AKI patients received CRRT during the stay of ICU.56.25%CRRT patients died in ICU. The 28-day mortality was 62.5%, and the 90-day mortality was 75%. The use of vasoactive agents, diagnosis of PCP were independent risk factors for predicting patients' death of CRRT in ICU. The cumulative survival of AKI 3 patients between CRRT and non-CRRT groups shows no significant differences.

Introduction

Acute kidney injury (AKI) is a common disease in critical patients and affects more than 13 million people all around the world annually[1]. Patients who are infected by Human Immunodeficiency Virus(HIV) are more vulnerable to suffer from AKI and probably have a higher mortality and morbidity[2, 3].66% HIV infected patients are diagnosed with AKI during stay in Intensive Care Unit(ICU)[4]. Continuous renal replacement therapy (CRRT) has been an important intervention in curing patients with severe AKI for more than one decade[5, 6]. However, few studies have clarified CRRT in patients with HIV/AIDS. Epidemiology and influence factors of CRRT in patients with HIV/AIDS are still unclear in China. This study aims to make these determinations among HIV-infected individuals in an observational retrospective clinical study.

Methods

Study design and population

It was a retrospective research in ICU of Beijing Ditan Hospital Capital Medical University which was a top three hospital majoring in infectious diseases. About five hundred patients were admitted in this general ICU and there were 20-bed ward for both medical and surgical patients each year. We reviewed the Hospital Information management System (HIS) from June 1,2005 to May 31,2017 in Beijing Ditan Hospital Capital Medical University in this research. All of the databases were recorded and analyzed by infectious specialists from our team. Patients who were clearly diagnosed with HIV and more than 18 years old were included in this study. Patients who underwent RRT before admission, stayed in ICU less than 48 hours and were admitted in ICU more than once within 6 months were excluded from this research. This study only recorded the first admission for patients who were admitted in ICU more than once within 6 months.

There were 284 cases admitted to ICU of Beijing Ditan Hospital Capital Medical University from June 1,2005 to May 31,2017. 47 cases were excluded because length of stay on ICU less than 48 hours. 4 cases were excluded by accepting renal replacement therapy before admission. Meanwhile 8 patients were recorded the first admission because of admitting in ICU twice within 6 months. 225 cases were brought into this research eventually.

Definitions

AKI diagnosis

We used the KDIGO criteria on diagnosing AKI. As the Kidney Disease Improving Global Outcomes (KDIGO) defined, AKI would be diagnosed if there was a 50% rise in serum creatinine from baseline at any point during the patient's prior 7-day ICU admission; a rise in serum creatinine of > 26.5 mmol/L within a 48-h period; a fall in urine output of < 0.5 mL/kg/h for more than 6 h; an absolute serum creatinine of > 353.6 mmol/L; or an RRT was initiated[7].

HIV diagnosis

As the US Centers for Disease Control and Prevention defined in revised surveillance case definition for HIV infection in 2014, HIV infected would be diagnosed when a positive result detected from an initial HIV antibody or combination antigen/antibody test, and accompanying or subsequent positive result detected from a supplemental HIV test different from the initial test[8]. Or patients with a positive result or report of a detectable quantity from any of the following HIV virologic tests:

- Qualitative HIV NAT (DNA or RNA)– Quantitative HIV NAT (viral load assay)
- HIV-1 p24 antigen test
- HIV isolation (viral culture) or
- HIV nucleotide sequence (genotype)[9]

Data collection

The following demographic, clinical, laboratory data, complication and multiple organs support therapy were collected from the patient medical manuals and an electronic hospital database by four investigators (H. Guo, L. Pu, J. Hao, and N. Yin): age, sex, body mass index, lymphocyte count, hemoglobin, albumin, t-bil, serum calcium, lactate, sodium bicarbonate, serum phosphate, GRF, MPV, ALT, AST, LDH, CD4 count at ICU admission, lowest CD4 count in ICU, HAART, PCP, septic shock, respiratory failure, the use of vasoactive agents, duration of mechanical ventilation, duration of CRRT.

The severity of illness was evaluated by the SOFA and APACHE II score, which calculation was based on the worst variables recorded within the first 24 h of ICU admission.

As the mode of all patients received CRRT was continuous venovenous hemodiafiltration (CVVHDF), therapeutic dose was 30 ml/kg, the related data were not recorded in this research.

Length of ICU stay and hospital are recorded by searching the Electronic Hospital Database.

Outcome measures

Outcome was recorded by searching the HIS of Beijing Ditan Hospital Capital Medical University. Follow-up visit was conducted by infectious specialists by telephone in this research.

Statistical analyses

Categorical variables were compared using a chi-squared test for trends. Risk factors were assessed by univariate analyses, and variables that were statistically significant ($p < 0.05$) in the univariate analyses were later included in a multivariate analysis. Univariate and multivariate analyses were performed using logistic regression. The life table method was used to determine survival curves, and a Cox proportional hazards model was used to evaluate the statistical differences between the survival and non-survival curves. Data presented as mean – standard deviation, median (interquartile range), percentage of number of cases, odds ratios (ORs) with 95% confidence intervals as appropriate. A two-tailed p -value < 0.05 was considered significant. Statistical analyses were performed using SPSS version 22.0 software (SPSS, Inc., Chicago, IL)

Results

Patient characteristics

Among the 225 patients, 205(91.1%) were male. The average age of the total numbers was 42 ± 13 years. 122(54.2%) patients were diagnosed with AKI during the stay in ICU, as the Figure 1 showed, the number and percentage of AKI stage 1/2/3 were respectively 38(31.1%)/23(18.9%)/61(50%). 32 patients (about 26.2% of total AKI) received continuous renal replacement therapy (CRRT) in ICU. 2 patients started CRRT in stage 2, the others ($n=30$) started in stage 3. 56.25% ($n=18$) of patients who received CRRT died in ICU.

Comparison between AKI patients with CRRT and without as the table 1, Hemoglobin and CD4 counts at ICU admission had statistically significant differences ($p = 0.048$ and $p = 0.043$, respectively). As for the complication, the incidence of pneumocystis carinii pneumonia (PCP) and respiratory failure showed significant statistical differences ($p = 0.006$ and $p = 0.01$, respectively). In severity of illness, patients with CRRT were even worse both in SOFA and APACHE-II score ($p \leq 0.001$, and $p \leq 0.001$, respectively). Patients with CRRT stayed hospital shorter than those without ($P = 0.022$).

As the figure 2 shown, 13 patients (40.6%) admitted to ICU for the reason of respiratory failure, 9 of them died in ICU. Secondly, 10 patients (31.25%) received treatment in ICU mainly because of occurring AKI, and only 2 of them died during stay in ICU. Septic shock, intestinal perforation, cardiopulmonary arrest, central nervous system disease consisted the rest reason admission to ICU.

Table 3 and table 4 respectively showed the strength of association between death in ICU and its potential risk factors calculated by univariate and multivariate logistics analysis. The result showed that respiratory failure, septic shock, the use of vasoactive agents, duration of mechanical ventilation, diagnosis of PCP, SOFA score at ICU admission, were respectively independent risk factors for CRRT by univariate logistics analysis.

Higher probability diagnosis of respiratory failure (OR=7.333, 95% CI 1.467-36.664, $p = 0.015$), higher probability diagnosis of septic shock (OR=1.005, 95% CI 1.001-1.010, $p = 0.018$), and higher probability to use vasoactive agents (OR=10.667, 95% CI 1.743-65.271, $p = 0.011$), longer mechanical ventilation duration (OR=1.011, 95% CI 1.002-1.019, $p = 0.011$), more probability to diagnose of PCP (OR=7.50, 95% CI 1.288-43.687, $p = 0.025$), higher SOFA score at ICU admission (OR=1.183, 95% CI 1.012-1.383, $p = 0.035$), longer duration of CRRT contributed to a higher mortality in ICU.

The multivariate logistics analysis showed the use of vasoactive agents, diagnosis of PCP and longer duration of CRRT were independent risk factors for predicting patients' death of CRRT in ICU. A higher probability to use vasoactive agents (OR=174.31, 95% CI 1.743-65.271, $p = 0.018$), more probability to diagnose PCP (OR=27.136, 95% CI 1.855-397.066, $p = 0.016$), longer duration of CRRT (OR=1.034, 95% CI 1.004-1.065, $p = 0.028$) contributed to a higher risk to die in ICU.

As the Figure 1 illustrated, most of AKI patients ($n = 30$, 93.75% of AKI patients) received CRRT in stage 3. Among the AKI 3 patients, about a half received CRRT during stayed in ICU. Then we compared the two groups in the table 2. Plasma-albumin and CD4 counts at ICU admission had statistically significant differences ($p = 0.046$ and $p = 0.007$, respectively). In severity of illness, patients received CRRT probably had a higher APACHE-II scores ($p = 0.019$). Even with the help of the CRRT, the main outcome such as the mortality in ICU and the renal recovery in the two groups did not show significant difference ($p = 0.373$ and $p = 0.437$, respectively). Patients received CRRT probably had a longer stay tendency in ICU ($p = 0.529$), but proved a shorter hospital stays ($p = 0.034$).

As the cumulative survival curves of HIV infected patients who were diagnosed with AKI 3 admitted to the intensive care unit shown in the Figure 3, the group of CRRT and non-CRRT had no significant difference

($p=0.309$). By the Cox Analysis for the cumulative survival of AKI 3 patients between the CRRT and non-CRRT groups as the table 5 clarified, the possibility of using vasoactive agents and duration of Mechanical ventilation shows significant difference on AKI 3 patients' survival ($p=0.014$, OR 2.501, 95% CI 1.205-5.192 and $p=0.006$, OR 0.998, 95% CI 0.997-0.999, respectively).

Discussion

Lin Pu has concluded that AKI occurred more than 50% on HIV-infected patients admitted to the ICU. Consistent with previous reports: the incidence of AKI for the patients admitted in ICU is 67% [10]. CRRT has practically and efficiently used in patients with AKI as a basic equipment [11, 12]. But the occurrence rate and influencing factors to predict patients' death of CRRT in ICU among Chinese is still unclear.

26.2% patients with AKI received CRRT during the stay of ICU in this research, significantly higher than 5–6% patients without HIV [2]. The result indicated that patients infected by HIV were more vulnerable to develop into severe AKI. Patients with HIV lost kidney function faster than the background population [13, 14]. Exposure to nephrotoxic drugs such as tenofovir and HIV replicating in other cells besides CD4 cells may aggravate deterioration of the renal function [15–17]. Rasch et al. concluded that the possibility of HIV patients receiving RRT were more than 4-fold compared with the background population without. Age, hypertension and AIDS were associated with the increased risk of RRT [15].

It had no difference with the former research illustrated: the mortality ranging from 37–88% for the patients admitted in ICU who need the RRT [18]. The study indicated that 56.25% of CRRT patients died in ICU. Mortality was higher in patients with HIV/AIDS, most likely due to the serious immunosuppression and opportunistic diseases [19]. Compared with survivals with CRRT, 15 patients of non-survivals suffered from the septic shock during the stay of ICU.

Patients who use vasoactive agents, diagnosis of PCP, a longer duration of CRRT are more probably to die in ICU. Ling ping et al. conclude that sepsis-related AKI and using vasopressors were independent risk factors to increase patients' mortality [20]. Dopamine and norepinephrine are two kinds of common vasopressors widely used in curing all kinds of shocks. Patients with septic shock are usually accompanied with hypotension and coagulopathy [21]. Then multiple organ syndrome occurred as a result of ischemia reperfusion injury. High vasoactive agents using might increase the risk of ICU death by the poor cardiovascular response to the catecholamine. Chou et al. concluded that critically ill patients being treated with a high dose of vasopressor also had a higher ICU mortality, CRRT didn't improve patients' prognosis [22].

Patients with HIV infection are more vulnerable to be influenced by opportunistic infections. PCP has been a common manifestation of HIV infection in developed country. It played an important role throughout the course of the disease and often as the initial manifestation of acquired immunodeficiency syndrome (AIDS) [23]. Meanwhile it resulted in lung injury and gas exchange by inducing pulmonary inflammatory response. Tumor necrosis factor- α and other immunomodulatory molecules were released as a response to the reaction of the infection [24, 25]. Prasad et al. found that patients with a higher FiO₂

requirements while ventilated and a higher vasoactive agent requirement were inclined to have an early(24 h) mortality[26]. PCP prophylaxis has been widely used in developed country[23], but still unpopularly used in developing country. Nearly no patients had vaccinated PCP prophylaxis in this research. On the other hand,25–33% patients were not diagnosed of PCP before they were clearly diagnosed of HIV[27]. Early diagnosis of HIV-infection and widely use of PCP prophylaxis perhaps contribute to decrease the mortality of CRRT.

This study deduced that a longer duration of CRRT made patients easier to die in ICU. Longer duration of CRRT meant more opportunities affected by catheter related bloodstream infection (CRSBI) and more vulnerability of CRRT related complication. Scott concluded in his research that there was no difference of pediatric survival rate between long and short duration CRRT[28]. The longer duration of CRRT, the higher risk of complication the patients might be. Patients in this article were all immunodeficiency, therefore any opportunity infection can be fatal for them.

The 28-day mortality of patients with CRRT was 62.5% in this research, matched for 62% in sepsis-induced acute kidney injury undergoing CRRT in previous reports[29].

As the Fig. 2 shown,13 patients of respiratory failure consisted the highest proportion of the ICU admission,10 (76.9%) patients died in ICU.10 patients of AKI consisted the secondary proportion of the ICU admission, only 2 (20%) died in ICU. 3 patients accepted the treatment in ICU because of septic shock,3 of total (75%) did not survive in ICU. The figure indicated that patients who were initially diagnosed with AKI probably had a better prognosis. On the contrary, the patients who were initially admitted in ICU for respiratory failure or septic shock, usually had a poor outcome compared with patients diagnosed with AKI and need the help of CRRT.

With the extensively use of highly active antiretroviral therapy (HAART), the survival of patients affected by HIV have been significantly improved[30]. The use of antiretroviral drugs is another influence factor to injure the renal function and increase the risk to accept the CRRT[31]. Previous researches indicated that both HIV infection and HAART were directly nephrotoxic[32–35]. We also acknowledged that only 30(24.6%) patients with AKI received the HAART during stay in ICU, there was no significant difference between CRRT group and non-CRRT group. The reason why most patients never received the HAART was that 71.1% patients were diagnosed with HIV infections within 3 months, so treatment had not started yet[36].

The count of CD4 + cell reflects the immune state of HIV patients. A former study has proved that CD4 count < 200 cells/ml was an independent predictor of experiencing AKI[37]. Low CD4 count, AIDS are risk factors for HIV-infected people suffering from AKI[38]. Lower CD4 count made HIV patients more vulnerable to suffer from opportunistic infections and increased the risk of kidney injury[36]. The average CD4 count of AKI patients was 23(8–78) cells/ml, and there was statistics difference ($p = 0.043$) between CRRT group 37(13–122) cells/ml and non-CRRT group 15(7–69) cells/ml. But there was no significant difference ($p = 0.464$) between CRRT survival group 97(25–156) cells/ml and CRRT non-survival group 40(15–110) cells/ml. CD4 count < 200 cells/ml meant a destroyed immune system condition, however,

there was no significant difference ($p = 0.245$ and $p = 0.863$) between CRRT group and non-CRRT group on sepsis and septic shock. The reason why there was no significant difference between the two groups on CD4 count is probably that the patients admitted to ICU were both suffering severe immunosuppression and easier to be infected by all kinds of pathogens. Franceschini et al. concluded that with the decreasing of patients' CD4 count, the possibility of morbidity and mortality extensively increased[37].

By using the Cox Analysis for the cumulative survival of AKI 3 patients between the CRRT and non-CRRT groups in Fig. 3, we concluded CRRT did not improve patients' long-term survival ($p = 0.309$). Without any doubt, CRRT had an exactly effect in maintaining the stability of the internal environment and decreasing pre load of heart and so on. The result indicated that AKI 3 might be not the proper stage to start the active intervention. Patients might benefit from early starting in AKI 1 or AKI 2.

Limitation:

The number of CRRT events is relatively small, which limits statistical power of analyses. This is a retrospective study. Thus, a large, prospective, randomized, controlled study is needed. As the mode of all patients received CRRT was continuous venovenous hemodiafiltration (CVVHDF), therapeutic dose was 30 ml/kg, the related data were not recorded in this research. Further research about different modes and therapeutic dose should be conducted and studied.

Conclusion:

The incidence of AKI was 54.2% in HIV-infected patients admitted to the ICU, and about 26.2% of AKI patients received CRRT during the stay of ICU. 56.25% CRRT patients died in ICU. The 28-day mortality was 62.5%, and the 90-day mortality was 75%. The use of vasoactive agents, diagnosis of PCP, longer duration of CRRT were independent risk factors for predicting patients' death of CRRT in ICU.

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Declarations

Ethical Approval and Consent to participate This study was approved by the Ethics Committee of Beijing Ditan Hospital, Capital Medical University, No.2018-005-01.

Consent for publication

Not applicable

Availability of supporting data

The data generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

AL and JYL designed the research scheme and provided research ideas. LP, JJH, NNY, YFL, HFX read the literature and collected medical records. HBG was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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Tables

Due to technical limitations, Tables 1-5 are provided in the Supplementary Files section.

Figures

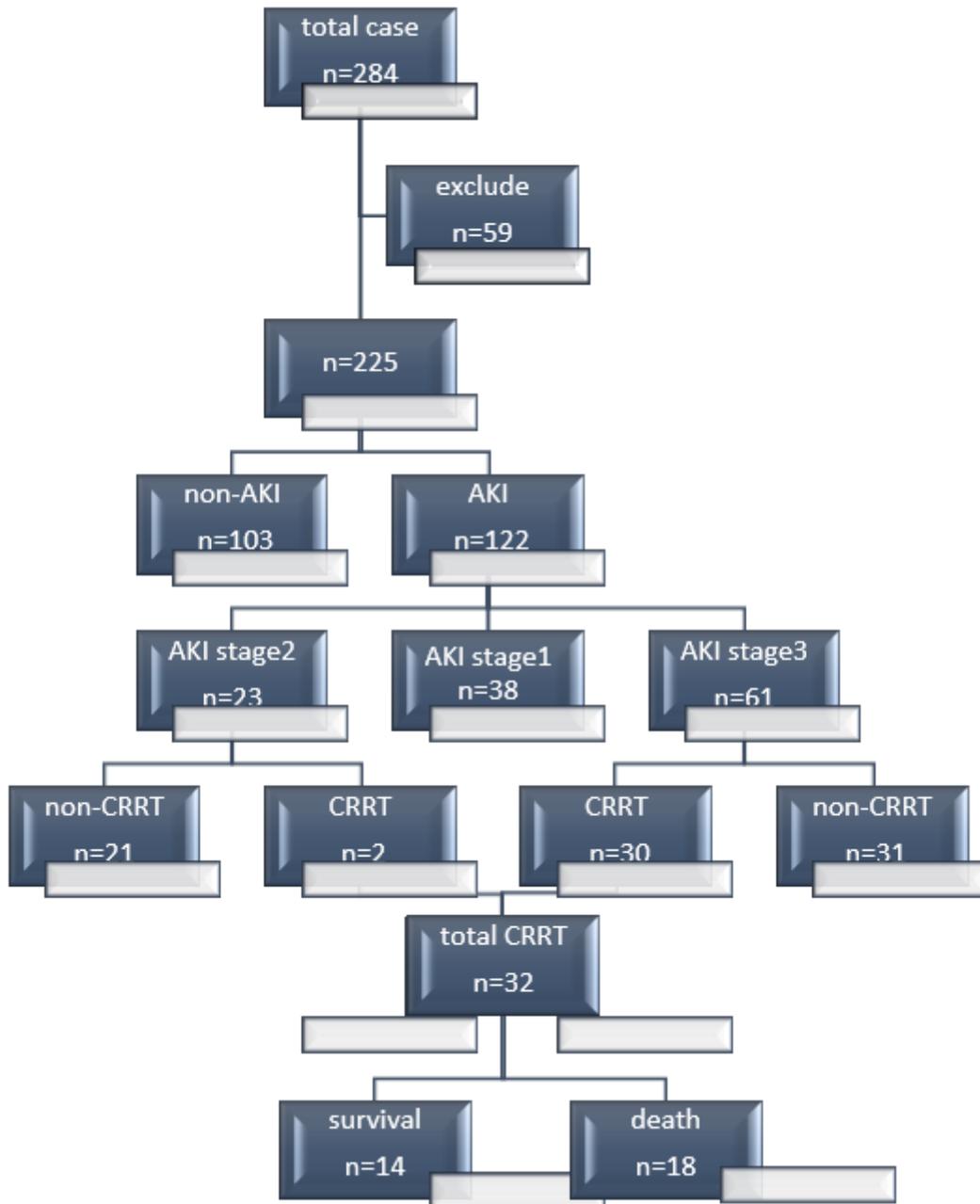


Figure 1

Study flow chart detailing the inclusion and exclusion of patients (June 3, 2005, to May 21, 2017). AKI, acute kidney injury; ICU, intensive care unit; CRRT, continuous renal replacement therapy; n, number. 59 patients were excluded: 47 patients were excluded as the length of stay in ICU \geq 48 hours; 8 were admitted more than once within 6 months; 4 underwent RRT before admission

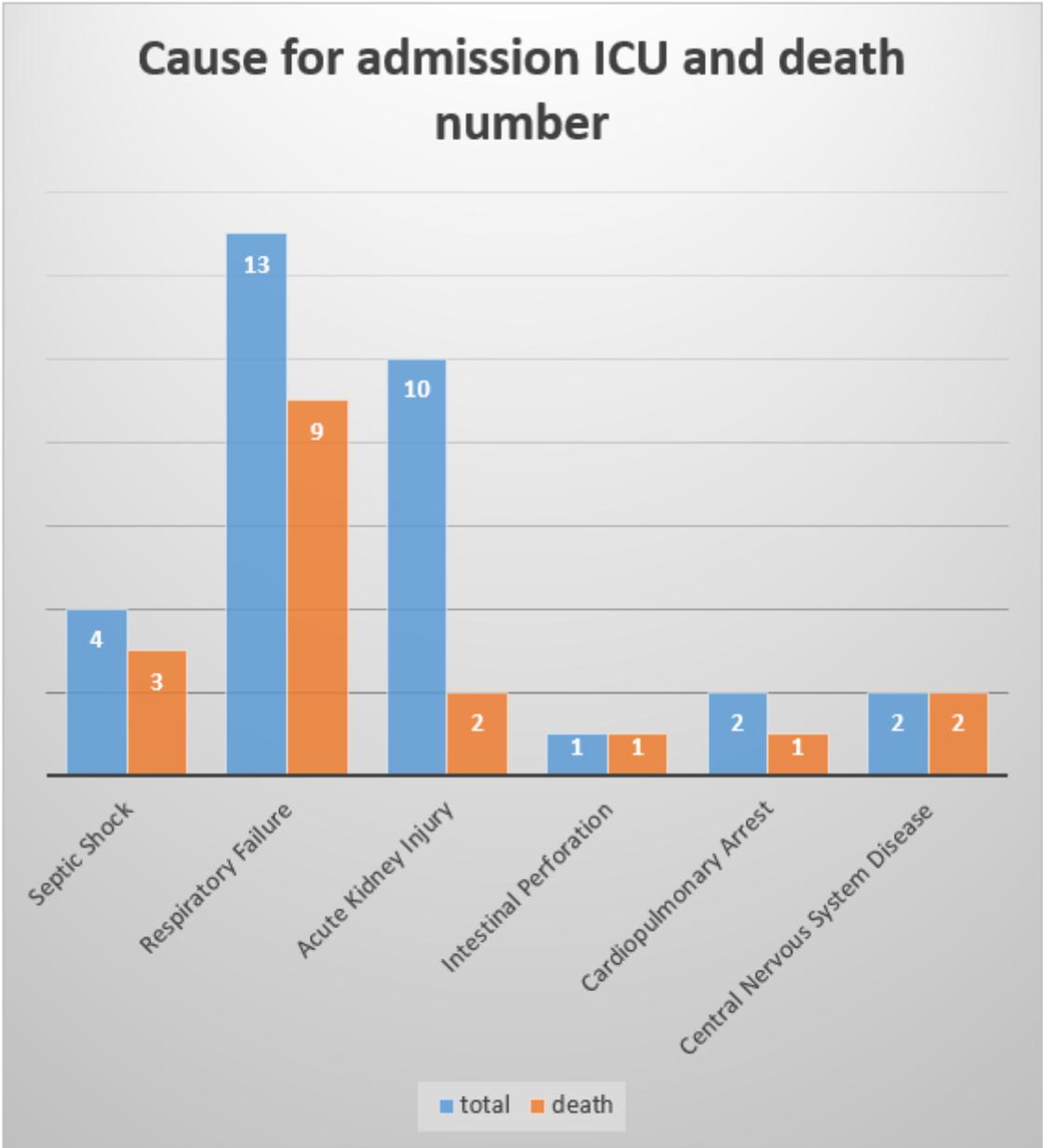


Figure 2

Cause for admission ICU and death number of the 32 CRRT patients. ICU, intensive care medicine; CRRT, continuous renal replacement therapy.

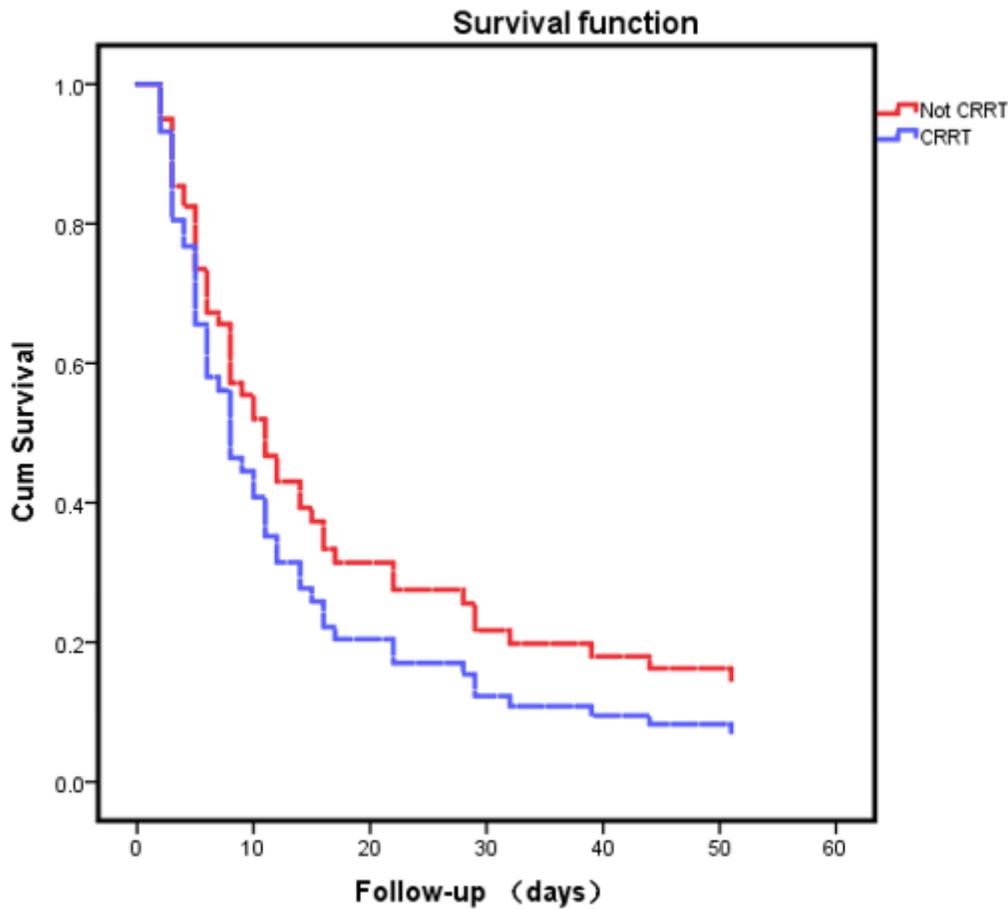


Figure 3

Cumulative survival curves of HIV infected patients who were diagnosed with AKI 3 admitted to the intensive care unit, received CRRT or not received (two groups). HIV, human immunodeficiency virus; CRRT, continuous renal replacement therapy. It shows no significant differences of survival between the group of CRRT and non-CRRT ($p = 0.309$).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [TABLE.docx](#)